The Transfusion System in Germany

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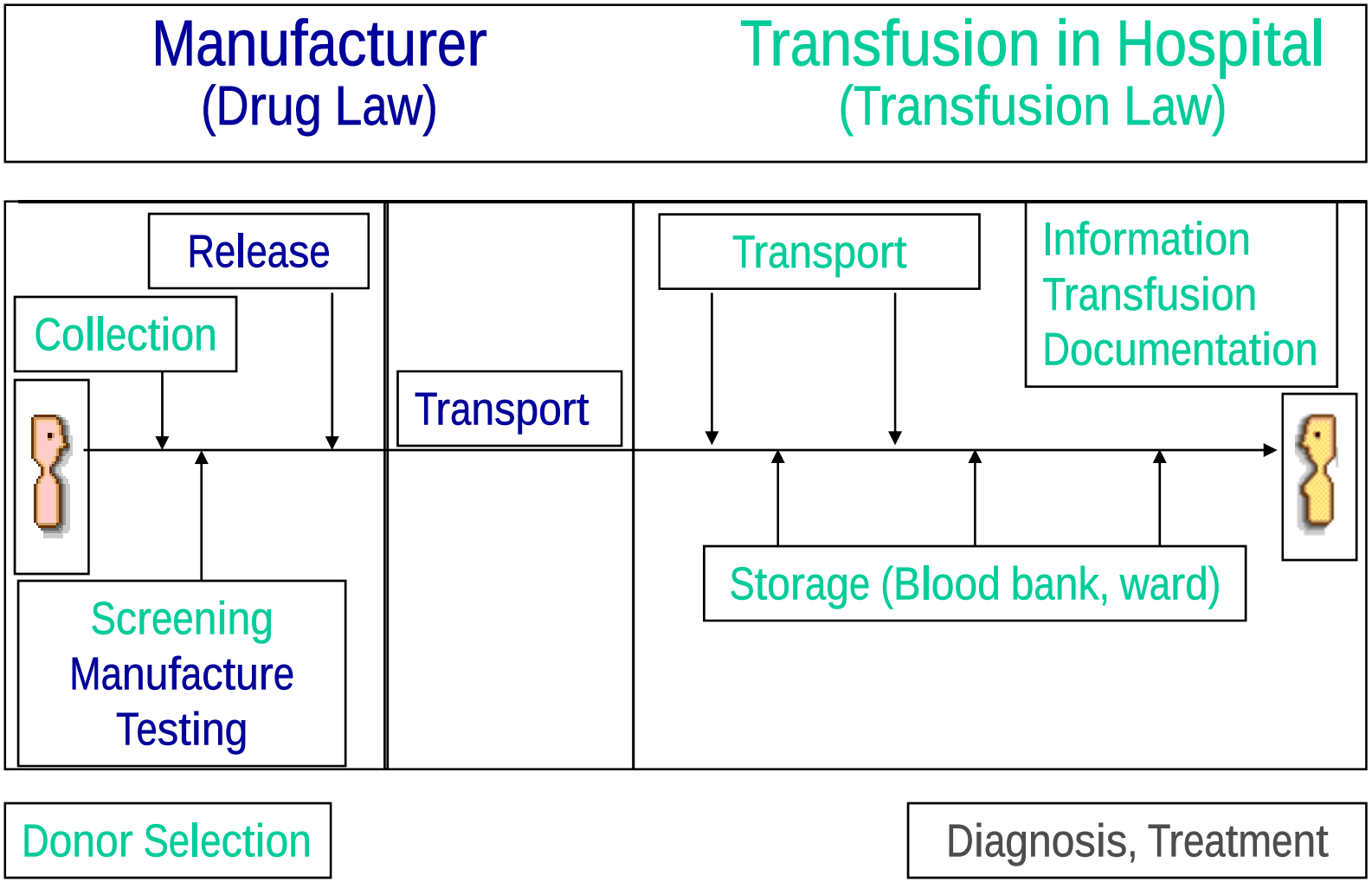
German Transfusion System Between AIDS shock and European Blood Directive

- Blood components considered as drugs (Drug act 1976):
  - Manufacturing license for blood establishments by regional authorities
  - GMP inspections by regional authorities
  - Individual marketing authorization for blood components by Paul-Ehrlich-Institut (PEI) as competent federal authority
  - Competence to impose mandatory requirements by PEI
  - Pharmacovigilance by PEI: collection and assessment of spontaneous notifications of suspected severe adverse drug reactions, line listing of non-severe adverse drug reactions
- IVD considered as drugs
  - Individual marketing authorization for IVD by PEI as competent authority
  - Batch release by PEI

Between AIDS shock and European Blood Directive

- Transfusion Act 1998, regulating basic requirements for
  - Donor information, protection, selection, and testing
  - Documentation of blood donation
  - Documentation of Use
  - Look back procedure
  - Notification of suspicion of severe and non-severe adverse reactions by blood establishments and physicians to PEI
  - Notification of the quantity of donation, manufacturing and use of blood products by blood establishments and physicians to PEI
  - Notification of donor epidemiology (HIV, HBV, HCV, Lues) by blood establishments to Robert Koch-Institute (RKI)
  - German Medical Association (BÄK), in liaison with the PEI, responsible for “Guidelines on the Collection of Blood and Blood Components and on the Use of Blood Products (Hemotherapy)”

Transfusion Chain



Cooperating parties for blood safety

Blood Establishments

Robert Koch-Institut

Epidemiology

German Medical Association

Guidelines

Hospitals

Paul-Ehrlich-Institut

Marketing Authorization
(blood components, ~~IVD~~)
Pharmacovigilance
IVD-Vigilance

31 Regional Authorities

Manufacturing Licenses
GMP inspections

National Advisory Committee Blood „AK BLUT“

- Members installed by the Ministry of Health represent
  - scientific societies,
  - different organizational structures of blood establishments,
  - medical disciplines involved in blood transfusion and treatment of hemophilia
  - Industry (Plasma Derivatives, IVD)
  - Patient groups
  - Federal authorities
  - PEI
- Main Tasks are
  - Discussion of actual opportunities and emerging threats
  - Preparing votes and opinions as a result of these discussions
  - Expert advice for Federal and Regional Authorities

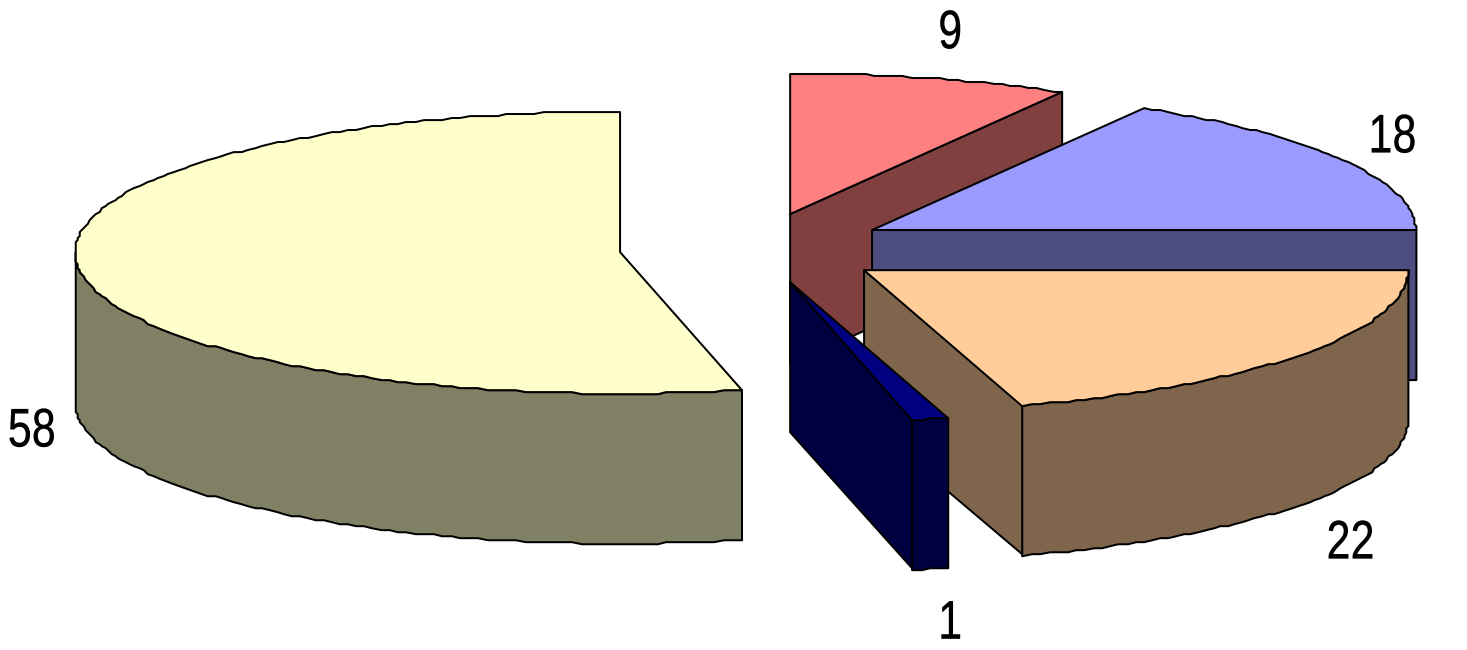
Research and Education as Main Pillars of Transfusion Safety

- Red cross and university blood establishments
  - Education of physicians, responsible for transfusion in hospitals
  - Research on hemostasis, immunhemotherapy, blood component quality, stem cell therapy, hereditary coagulation disorders, blood component safety, donor epidemiology
- Paul-Ehrlich-Institute
  - Research on hemostasis, blood component quality and safety, donor epidemiology, hemovigilance - often done in co-operation with blood establishments
- Robert Koch-Institute
  - Research on donor epidemiology
- Co-operation of scientists under the head of AK Blut
  - Relevance of different blood-borne pathogens for blood product safety, standardized review publications on:
    CJD, vCJD, HIV, HBV, HCV, HAV, HCMV, HEV, HTLV, GBVC, Treponema, Yersinia, Parvovirus B19, TTV, Coxiella burnetii, influenza, arbobacteria, arboviruses

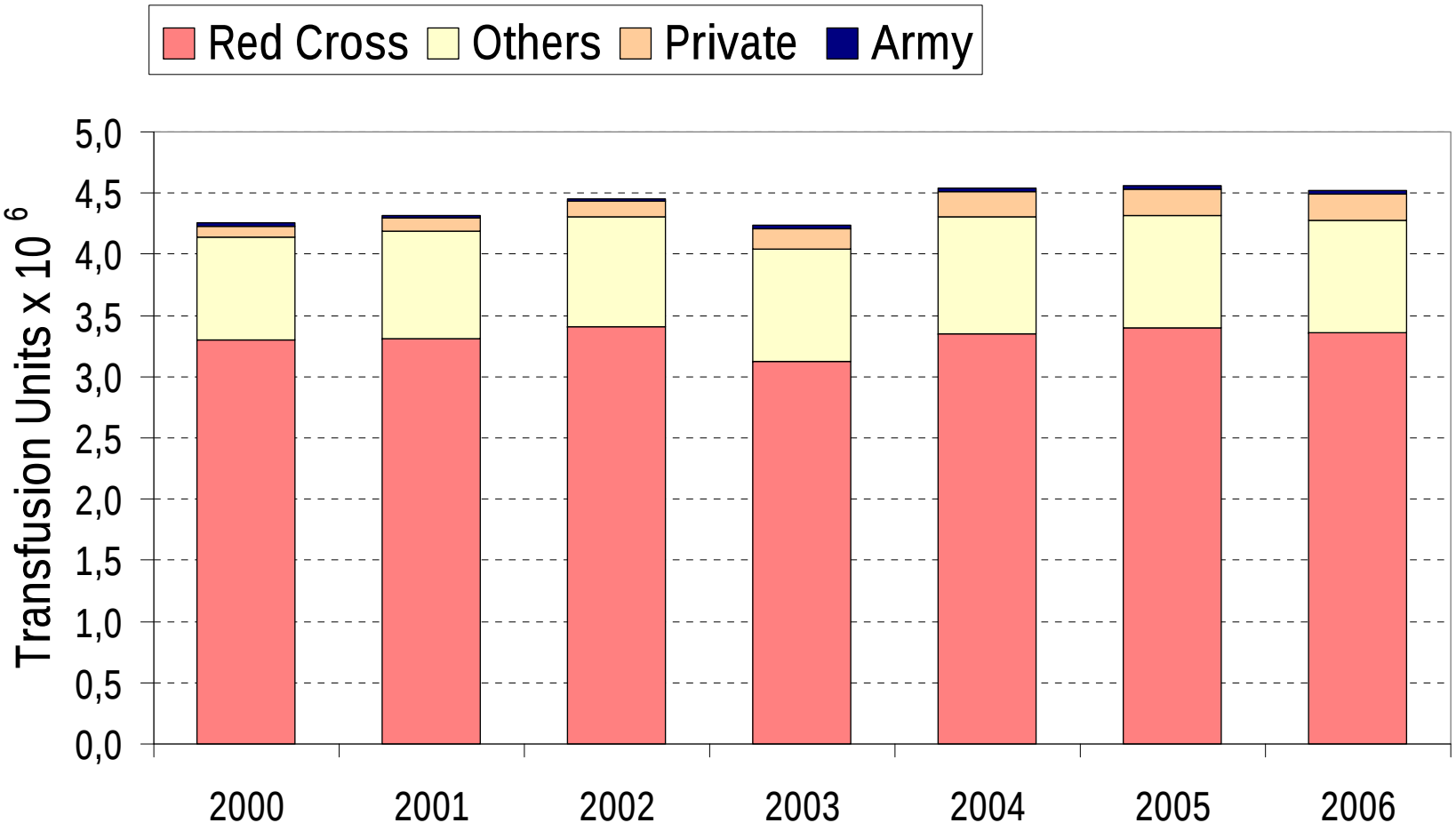
German Transfusion System and European Legislation regulating blood components

- 93/42/EC Medical Devices – standards for blood bags systems
- 98/79/EC In-Vitro-Diagnostics – standards for screening tests - Licensing and batch release by PEI ceased ► Loss of control
- 2002/98/EC Standards of quality and safety for collection, testing, processing, storage, distribution of blood components –hemovigilance
  2004/33/EC Technical requirements for blood components
- 2005/61/EC Look-back and Hemovigilance – requirement of annual notification to the commission of
  - serious adverse events which may influence product quality and safety
  - serious adverse reactions which may be due to product quality and safety
- 2005/62/EC Quality system

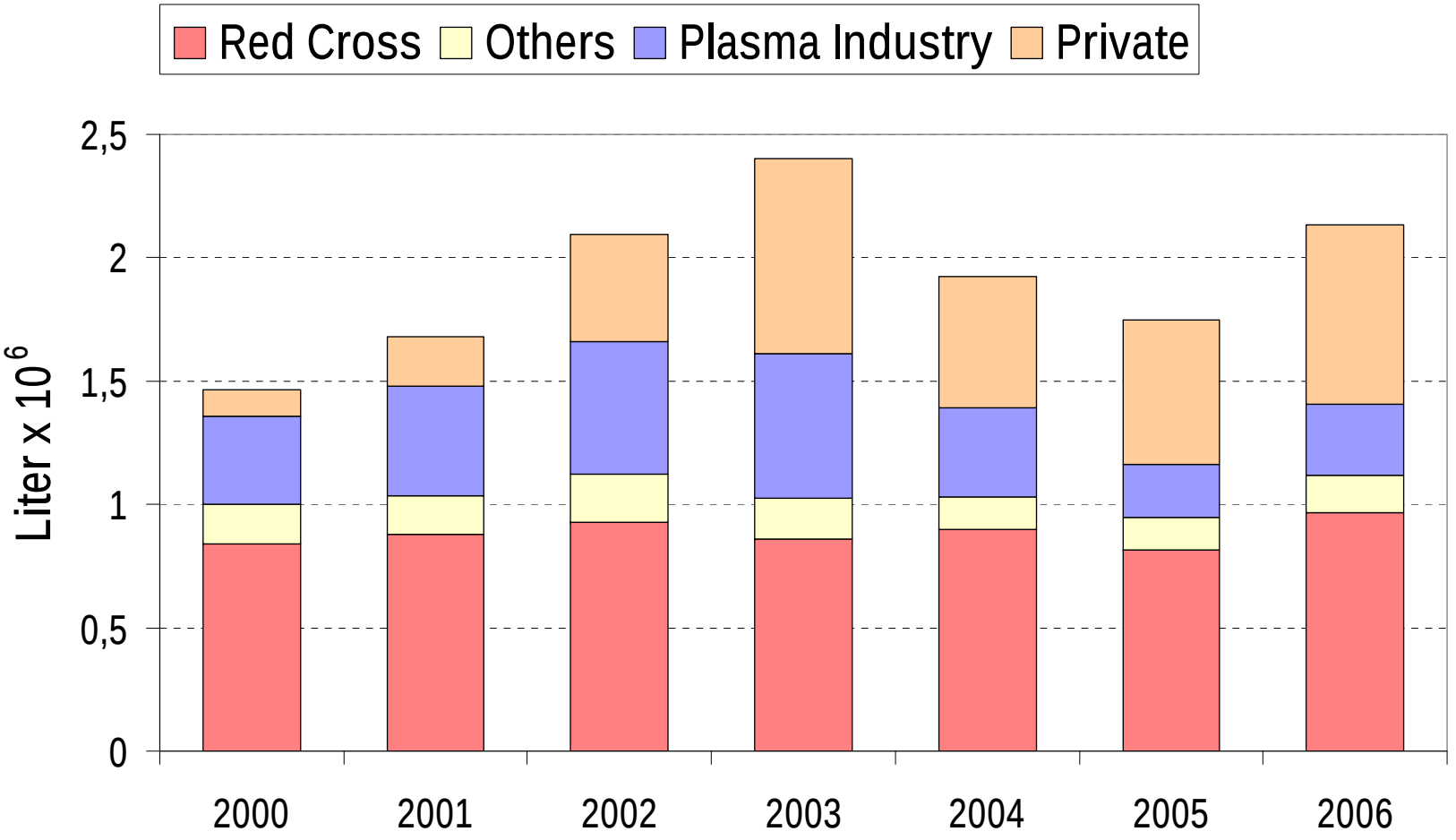
Different Organizational Structures of Blood establishments in Germany (2007)



RBC Processing from Whole Blood Donation and Apheresis by blood establishments of different structures



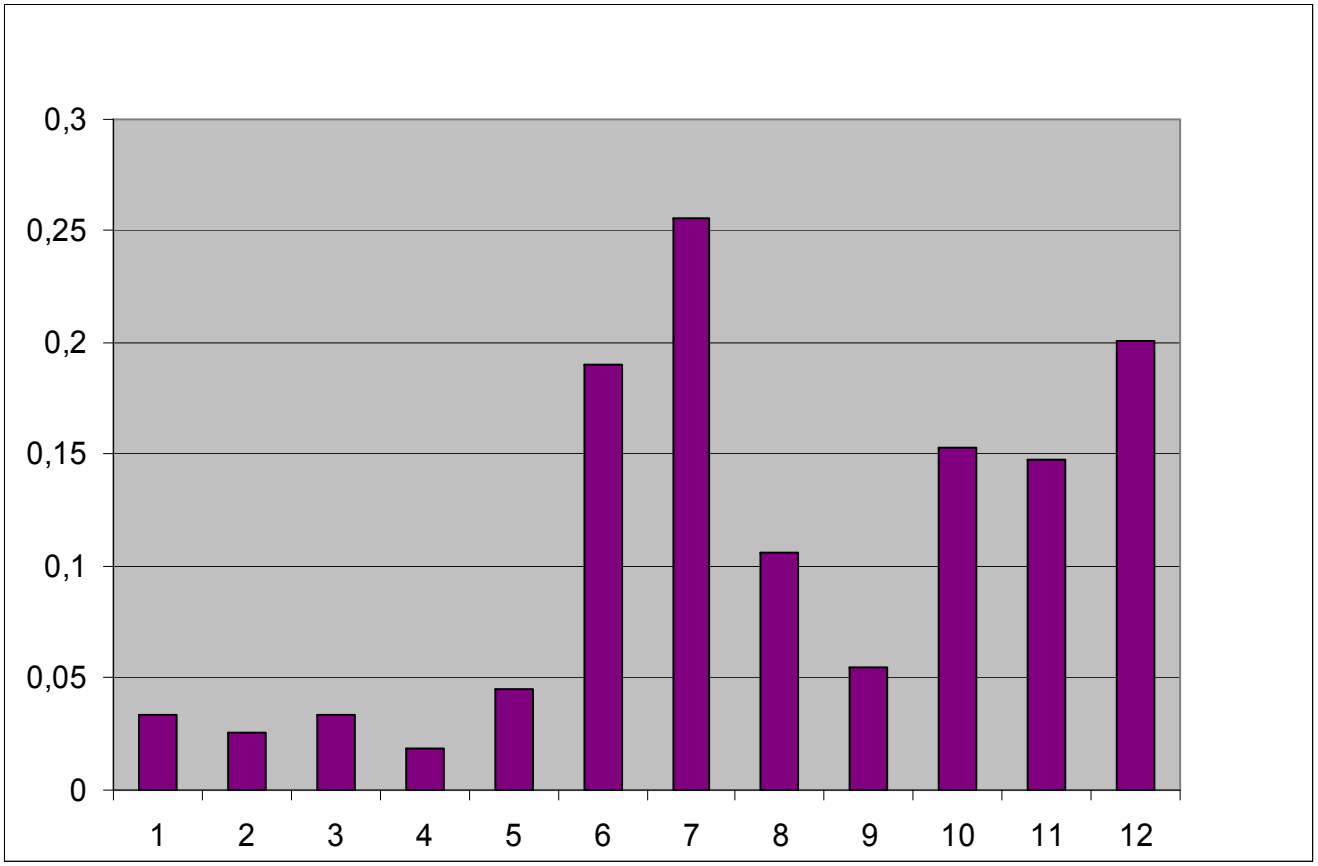
Plasma for fractionation (Whole blood donation and apheresis): Collection by blood establishments of different structures



Average Blood Supply

- 2005-2006 average for Germany
  - 57 Whole Blood donations per 1000 inhabitants
  - 53 RBC provided per 1000 inhabitants
- 2004 average for European Countries
  - 37 Whole Blood donations per 1000 inhabitants
  - 37 RBC provided per 1000 inhabitants

Practical Experience:
Percentage of refused Requests for RBC (Red Cross West 2006)



Answer: Optimal Use?

Blood Safety

Average annual number of blood components distributed in Germany from 2000 to 2006

RBC	4,412,900
PC	404,400
FFP	1,227,200
Total/year	6.044,500

Transfusion transmitted viral infections from 1994 to 2007, assessed as probable

HIV	7
HBV	53
HCV	34
Total/14years	84

Transfusion transmitted bacterial infections, assessed as probable

Products involved	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006
RBC: 26	4 (2)	5 (2)	1	0	4	3	2	2	3	2
PC: 32	0	2	4	2 (1)	4	3 (1)	4 (1)	3 (1)	6 (1)	4
FFP: 5	0	4	0	0	0	0	0	1	0	0
Sum: 63	4	11	5	2	8	6	6	6	9	6

All but one (day 4) of fatal PC transmissions were transfused on day 5 of storage.

- 9 deaths caused by 6 PC, and 4 RBC, i.e., one patient died on average per year and per 400,000 PC administered.

Pathogen reduced Blood Components despite an extremely low risk of transfusion transmitted pathogens?

- Pathogen inactivation of blood components is not required as a nation wide measure with respect to risk of HIV, HCV, HBV transmission.
- However, establishments can apply for a marketing authorization of pathogen inactivated blood components.
- Possible gain in platelet safety despite infectivity against spores?
- Adding to the already high safety achieved by pathogen screening (e.g. in case of errors or test failures)
- Preparedness in case of new emerging diseases / pandemic without test available

Ultimate Goal

- Supply of blood products to meet the needs of patients
  - in sufficient amount,
  - with good quality,
  - with reliable efficacy,
  - with an acceptable safety.
- To achieve this object is in the responsibility of
  - manufacturers,
  - official regulatory bodies.